```
     (FILE 'HOME' ENTERED AT 16:37:55 ON 03 MAY 2002)

     FILE 'REGISTRY' ENTERED AT 16:38:04 ON 03 MAY 2002
L1             1 S SODIUM TETRABORATE/CN
L2             1 S AMMONIUM HYDROXIDE/CN

     FILE 'CAPLUS, BIOSIS, USPATFULL' ENTERED AT 16:39:05 ON 03 MAY 2002
L3        393633 S L2 OR (AMMONIUM HYDROXIDE) OR (NH4 OH) OR NH4OH OR (AMMONIA
W
L4         20420 S (ANHYDROUS BORAX) OR (BORAX GLASS) OR (DISODIUM
TETRABORATE)
L5           145 S L3 (20W) L4

     FILE 'REGISTRY' ENTERED AT 16:46:10 ON 03 MAY 2002
L6           284 S ALGINATE

     FILE 'USPATFULL, CAPLUS, BIOSIS' ENTERED AT 16:46:24 ON 03 MAY 2002
L7         66517 S L6 OR ALGIN?
L8            16 S L7 AND L5
L9            48 S L5 AND (SPONGE OR GEL OR HYDROGEL OR PAD OR FOAM OR DRESSING
L10           38 S L9 NOT L8

=>  log hold
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     FILE 'REGISTRY' ENTERED AT 15:08:24 ON 03 MAY 2002
L11             1 S SODIUM TETRABORATE/CN
L12             1 S AMMONIUM HYDROXIDE/CN
L13             1 S SODIUM ALGINATE/CN
L14             1 S SODIUM CARBONATE/CN
L15             1 S SODIUM BICARBONATE/CN
L16             1 S ACETIC ACID/CN
L17             1 S LACTIC ACID/CN
L18             1 S MALIC ACID/CN
L19             2 S GLUCONIC ACID/CN
L20             2 S ASCORBIC ACID/CN
L21             1 S GLYCERIN/CN
L22             1 S PROPYLENE GLYCOL/CN
L23             1 S ETHYLENE GLYCOL/CN
L24             1 S POLYETHYLENE GLYCOL/CN
L25             1 S POLYOXYETHYLENE SORBITAN MONOOLEATE/CN
L26             0 S POLYOXYETHYLENE SORBITAN TRIOOLEATE/CN
L27             0 S POLYOXYETHYLENE SORBITAN TRIOLEATE/CN
L28             1 S POLYOXYETHYLENE SORBITAN MONOPALMITATE/CN

     FILE 'CAPLUS, USPATFULL' ENTERED AT 15:12:51 ON 03 MAY 2002
L29         61407 S L11 OR L12 OR (SODIUM TETRABORATE) OR (AMMONIUM HYDROXIDE)
L30         37761 S L13 OR L1 OR ALGINATE
L31        118464 S L14 OR L15 OR (SODIUM CARBONATE) OR (SOCIUM BICARBONATE)
L32        456727 S L16 OR L17 OR L18 OR L19 OR L20 OR (ASCORBIC ACID) OR
(ACETIC
L33        115297 S L25 OR L28 OR SORBIT?
L34            20 S L29 (20W) L30
L35             0 S L34 AND L31
L36         47852 S L20 AND L32
L37            14 S L34 AND L32
L38             6 S L34 NOT L37
```

L38 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:943718 CAPLUS
DOCUMENT NUMBER: 123:321743
TITLE: Air freshener gel manufactured with alginate and borate
INVENTOR(S): Fitzpatrick, John Patrick; Solanki, Yogesh
PATENT ASSIGNEE(S): Kelco International Ltd., UK
SOURCE: Brit. UK Pat. Appl., 15 pp.
CODEN: BAXXDU
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2286531	A1	19950823	GB 1994-2992	19940217

L38 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1976:137565 CAPLUS
DOCUMENT NUMBER: 84:137565
TITLE: Alkylene glycol alginates
INVENTOR(S): Strong, Clifford H.
PATENT ASSIGNEE(S): Uniroyal Ltd., Can.
SOURCE: Ger. Offen., 47 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2529086	A1	19760129	DE 1975-2529086	19750630
DE 2529086	B2	19791213		
DE 2529086	C3	19800821		
CA 1019326	A1	19771018	CA 1974-204887	19740716
US 3948881	A	19760406	US 1974-518126	19741025
NO 7502170	A	19760119	NO 1975-2170	19750618
NO 140719	C	19791024		
NO 140719	B	19790716		
JP 51019800	A2	19760217	JP 1975-78471	19750624
DK 7503210	A	19760117	DK 1975-3210	19750715
FR 2278706	A1	19760213	FR 1975-22110	19750715
ES 439475	A1	19770201	ES 1975-439475	19750716
PRIORITY APPLN. INFO.:			CA 1974-204887	19740716

L38 ANSWER 3 OF 6 USPATFULL
ACCESSION NUMBER: 92:61580 USPATFULL
TITLE: High molecular weight colloids which control bleed
INVENTOR(S): Moffatt, John R., Corvallis, OR, United States
PATENT ASSIGNEE(S): Hewlett-Packard Company, Palo Alto, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5133803		19920728	
APPLICATION INFO.:	US 1991-737101		19910729	(7)
DISCLAIMER DATE:	20090421			

7 ANSWER 1 OF 14 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:405476 CAPLUS
DOCUMENT NUMBER: 127:35884
TITLE: Water-soluble alginate salt fibers and their manufacture using reduced amounts of organic solvents
INVENTOR(S): Okamoto, Akira; Fukuyose, Yasuji; Yamazaki, Masakatsu
PATENT ASSIGNEE(S): Daiwabo Rayon Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 4 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 09119023	A2	19970506	JP 1995-303619	19951026

AB Title fibers, useful for medical goods, etc., show dry strength .gtoreq.0.5 g/denier. The fibers are manufd. from water-based dopes contg. water-sol. alginate salts by extrusion into acids and impregnation with hydroxides of ions providing water soly., which are dissolved in aq. org. solvents. Fibers of enhanced water soly. can be manufd. in the process with safety. Thus, a 4% dope of Na alginate was spun into H2SO4 bath, impregnated with a mixt. of NaOH 8, water 8, and MeOH 84%, washed by 35:65 mixt. of water and MeOH, and dried to give a 4.3-denier fiber showing tensile strength 0.63 g/denier and elongation 10.7%.

L37 ANSWER 2 OF 14 USPATFULL

ACCESSION NUMBER:	2001:51555 USPATFULL
TITLE:	Process for the preparation of aqueous dispersions of particles of water-soluble polymers and the particles obtained
INVENTOR(S):	Vanderhoff, John W., Bethlehem, PA, United States Lu, Cheng Xun, Somerset, NJ, United States Lee, Clarence C., Lilburn, GA, United States Tsai, Chi-Chun, Lawrenceville, GA, United States
PATENT ASSIGNEE(S):	C. R. Bard, Inc., Murray Hill, NJ, United States (U.S. corporation) Lehigh University, Bethlehem, PA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6214331	B1	20010410
APPLICATION INFO.:	US 1997-989888		19971212 (8)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1996-659770, filed on 6 Jun 1996, now abandoned Continuation-in-part of Ser. No. US 1995-466676, filed on 6 Jun 1995, now abandoned		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Kulkosky, Peter F.		
LEGAL REPRESENTATIVE:	Kilpatrick Stockton LLP		
NUMBER OF CLAIMS:	29		
EXEMPLARY CLAIM:	1		
LINE COUNT:	3840		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention is a process for the preparation of crosslinked water-swellable polymer particles. First, an aqueous polymer solution containing a water-soluble polymer having at least one functional group or charge, is combined with aqueous medium. The aqueous polymer solution is then mixed under moderate agitation with an oil medium and an emulsifier to form an emulsion of droplets of the water-soluble polymer. A crosslinking agent capable of crosslinking the functional groups and/or charges in the water-soluble polymer is then added to the

PATENT INFORMATION: US 3898986 19750812
APPLICATION INFO.: US 1972-319014 19721227 (5)
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Gaudet, Richard A.
ASSISTANT EXAMINER: McGowan, J. C.
LEGAL REPRESENTATIVE: Sabatine, Paul L., Mandell, Edward L., Benz, William H.
NUMBER OF CLAIMS: 16
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 7 Drawing Figure(s); 3 Drawing Page(s)
LINE COUNT: 1120
AB An improved intrauterine device which delivers a predetermined therapeutically effective dosage of drug locally to the uterus over a defined period of time is disclosed. The device is initially of a uterine-retentive shape. The device is characterized by undergoing a structural biotransformation in the uterus such that at the completion of the defined period of drug delivery it has achieved a non-uterine-retentive configuration.

L37 ANSWER 14 OF 14 USPATFULL
ACCESSION NUMBER: 75:30676 USPATFULL
TITLE: Erodible intrauterine device
INVENTOR(S): Ramwell, Peter W., Palo Alto, CA, United States
PATENT ASSIGNEE(S): Alza Corporation, Palo Alto, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 3888975		19750610
APPLICATION INFO.:	US 1972-318890		19721227 (5)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Rose, Shep K.
LEGAL REPRESENTATIVE: Sabatine, Paul L., Benz, William H., Mandell, Edward L.
NUMBER OF CLAIMS: 2
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 7 Drawing Figure(s); 3 Drawing Page(s)
LINE COUNT: 970
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB An intrauterine device for administering drug locally to the uterus at a controlled rate for a prolonged period of time is disclosed. The device contains a body of polymer capable of bioeroding in the environment of the uterus over a prolonged period of time. This body has the drug dispersed throughout so that as the body gradually bioerodes, it slowly releases the dispersed drug. In a preferred embodiment, the device releases a uterine contraction-inducing prostaglandin locally to the uterus at a controlled rate over a prolonged period of time.

=> d kwic 1-2, 9 5 3

L37 ANSWER 1 OF 14 CAPLUS COPYRIGHT 2002 ACS
IT 1309-42-8, Magnesium hydroxide 1310-58-3, Potassium hydroxide, uses 1310-73-2, Sodium hydroxide, uses **1336-21-6**, **Ammonium hydroxide**
RL: MOA (Modifier or additive use); USES (Uses)
(for enhancement of water soly. of **alginate** salt fibers)

L37 ANSWER 3 OF 14 USPATFULL

ACCESSION NUMBER: 2001:44254 USPATFULL

TITLE: Compositions and methods for the prophylaxis and treatment of dysmenorrhea, endometriosis, and pre-term labor, using histidine

INVENTOR(S): Peterson, John, Dickinson, TX, United States
Thomas, Peter G., Charlottesville, VA, United States

PATENT ASSIGNEE(S): Cytos Pharamaceuticals, LLC, Durham, NC, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6207696	B1	20010327
APPLICATION INFO.:	US 1998-153354		19980915 (9)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Jordan, Kimberly
LEGAL REPRESENTATIVE: Petraglia, Susan, Angres, Isaac
NUMBER OF CLAIMS: 61
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 8 Drawing Figure(s); 8 Drawing Page(s)
LINE COUNT: 1333
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to methods and compositions for preventing or treating conditions or disorders of the female reproductive system by administering an effective dosage of histidine alone or in combination with other therapeutic agents. The invention relates also to novel physical compositions and delivery devices for administering histidine effectively to a female subject in need of either prophylaxis or treatment of certain disorders of the reproductive system.

L37 ANSWER 3 OF 14 USPATFULL

SUMM . . . NSAIDS and all demonstrate, in varying degrees, the ability to inhibit prostaglandin synethesis. These include aryl carboxylic and arylalkanoic acids, **acetic acid** analogs, propionic acid analogs, fenamates, and enolic acids (including pyrazolidinediones). While NSAIDS are predominantly the treatment of choice for primary. . .

DETD . . . and calcium, respectively, salts if mineral acids such as HCl and sulfuric acid, or salts of organic acids, such as **acetic acid**. Amine addition salts may also be used in the practice of the invention, for example a phosphate amine addition salt.. . .

DETD . . . hydrophilic substances include ethylene-glycol acrylate, ethylene-glycol methacrylate, acrylamide, methacrylamide, acrylamide methylol, acrylamide diacetone or an unsaturated acidic product such as **malic acid**, acrylic acid, methacrylic acid, fumaric acid, itaconic acid or propylene glycol acrylate or methacrylate. Also polypropylene, polyamides, polyesters such as. . .

DETD . . . specified number of moles of histidine to obtain the desired dose in sterilized water while stirring the solution to homogeneity. **Acetic acid** is added to the resulting aqueous solution of histidine to adjust the same to a pH of 7.0. The resulting. . .

DETD B) A combination therapy ready-for-use i.v. solution containing 0.2% ciprofloxacin and 10% L-histidine in a 5% dextrose solution, solubilized with **lactic acid**, and pH adjusted with HCl.

DETD 2. The resulting white paste is slowly poured into 100 ml of 1.2% **ammonium hydroxide** solution under vigorous agitation. To this suspension is added 10 grams of zinc **alginate** previously prepared, and the vigorous agitation is continued until the complete dissolution of the zinc alginate results; if marked thickening.

. .

L37 ANSWER 5 OF 14 USPATFULL

ACCESSION NUMBER:	92:88877 USPATFULL
TITLE:	Storage stable aqueous soluble germicidal film forming composition
INVENTOR(S):	Greenwald, Richard B., Eagan, MN, United States Halsrud, David A., Minneapolis, MN, United States
PATENT ASSIGNEE(S):	Ecolab, Inc., St. Paul, MN, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5158766		19921027
APPLICATION INFO.:	US 1990-545768		19900628 (7)

RELATED APPLN. INFO.:	Continuation of Ser. No. US 1989-337336, filed on 13 Apr 1989, now abandoned
DOCUMENT TYPE:	Utility
FILE SEGMENT:	Granted
PRIMARY EXAMINER:	Page, Thurman K.
ASSISTANT EXAMINER:	Kulkosky, Peter F.
LEGAL REPRESENTATIVE:	Merchant, Gould, Smith, Edell, Welter & Schmidt
NUMBER OF CLAIMS:	46
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	2 Drawing Figure(s); 2 Drawing Page(s)
LINE COUNT:	691

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A single-part aqueous, storage stable, antimicrobial film-forming composition comprising a major portion of water, an antimicrobially effective amount of a cationic germicidal agent having the structure

(R)

(R.sub.1) (R.sub.2) (R.sub.3) N.sup.+ X.sup.-, wherein R, R.sub.1, R.sub.2, and R.sub.3 are independently selected from groups including benzyl, alkyl, benzyl, halo benzyl, C.sub.1-14 alkyl, C.sub.5-24 alkyl or C.sub.1-4 hydroxyalkyl and X.sup.- represents an anion capable of imparting water solubility or dispersability to the compound, and a stoichemetrically effective amount of acid functional anionic polymer, wherein said cationic germicidal agent and anionic polymer remain

pH adjusted with concentrated ammonium hydroxide or **acetic acid

DETD . . . 250-212 um 6.9 3.4
c. 212-150 um 35.3 24.2
d. <150 um 51.2 48.6
*0.75 .times. 10.sup.6
pH adjusted with concentrated ammonium hydroxide or **acetic acid

DETD Wash the gel sequentially with 2.times.100 ml water, 100 ml 0.1 M **acetic acid**, 100 ml water, 100 ml 0.1 M NaOH, 100 ml 0.5 M NaCl, and 100 ml PBS.

L37 ANSWER 9 OF 14 USPATFULL

DETD . . . by condensing the corresponding dibasic acid or anhydride in the presence of SOCl.sub.2, benzene and a lower alkyl ester of **acetic acid** such as ethyl acetate. Alternatively, the desired dibasic acid or anhydride thereof can be mixed with acetic anhydride to form. . .

DETD wherein n has a value of 1 or 2 especially **lactic acid** and glycolic acid. Also included are copolymers derived from mixtures of these acids. The preparation of polymers of the formula. . .

DETD 2. The resulting white paste is slowly poured into a Waring blender containing 100 ml of 1.2% **ammonium hydroxide** solution under vigorous agitation. To this suspension is, then, added 5 grams of zinc **alginate** previously prepared, and the vigorous agitation is continued until the complete dissolution of the zinc alginate results; if marked thickening. . .

DETD 1. Poly(**lactic acid**) is prepared from the cyclic lactide as described by R. K. Kulkarni, E. G. Moore, A. F. Hegyelli, and F.. . .

L37 ANSWER 5 OF 14 USPATFULL

DETD . . . can be removed by treatment with dilute concentrations of organic or inorganic acids such as HCl acid, sulfuric acid, or **acetic acid**, among others.

DETD . . . active itaconic/acrylic acid (about 1:3 mole ratio) copolymer was diluted to a total of 80 grams with distilled water. Concentrated **ammonium hydroxide** was then added to the mix until the pH was 8. 6.4 grams of a sodium **alginate** thickener known as Kelgin XL was added to the mix with stirring until a homogeneous paste was obtained. While stirring,. . .

IT **64-19-7, Acetic acid**, uses 144-62-7, Oxalic acid, uses 7647-01-0, Hydrochloric acid, uses 7664-38-2, Phosphoric acid, uses 7664-93-9, Sulfuric acid, uses 7697-37-2, Nitric acid, uses
RL: NUU (Other use, unclassified); USES (Uses)
(for spinning water-sol. alginate salt fibers)

L37 ANSWER 2 OF 14 USPATFULL
DETD The **ammonium hydroxide** was added to a 5% aqueous solution of sodium **alginate** containing XAMA-7 pentaerythritol-tris-[beta-(N-aziridinyl)-propionate] crosslinking agent
to adjust the pH to pH 11. With this crosslinking agent, this pH adjustment is. . . the crosslinking agent. Once the emulsion was formed and the desired droplet size distribution was achieved, a small amount of **acetic acid** was added to lower the pH to 7-8. The sodium alginate droplets crosslink rapidly at this lower pH. The crosslinked. . .

DETD . . .	11.6	23.5	14.7	11.8	26.9	8.3	
<150 um	70.3	79.0	60.3	70.1	80.6	82.2	76.6

*after addition of ammonium hydroxide
after addition of **acetic acid
DETD . . . alginate phase with ammonium hydroxide to pH 11, forming the water-in-oil emulsion, and subsequently lowering the pH to 7-8 with **acetic acid** to initiate rapid crosslinking of the polymers in the droplets to form polymer particles.
DETD . . . water-in-oil emulsion was monitored by optical microscopy while
the emulsion was being stirred. When the emulsion was judged satisfactory, sufficient **acetic acid** was added to decrease the pH of the aqueous phase to 7-8. This mixture was then stirred for about 4-5. . .
DETD . . . 10.50
pH (controlled by addition of 30% ammonium hydroxide) 10-11
Toluene 150.00
SPAN 60 emulsifier 1.50
XAMA-7 crosslinking agent 6.00
pH (controlled by addition of 10% **acetic acid**) 7-8
Isopropanol dehydrating agent 150.00
DETD . . . droplet size was monitored by optical microscopy while the emulsion was being stirred. When it was deemed satisfactory, sufficient 10% **acetic acid** was added to lower the pH of the aqueous phase to 7-8. This mixture was then stirred for 6 hours. . .

DETD . . . good			
after pH 7-8**	good	good	good
small particles***	++ + ++		
irregular particles***	++ ++ +		

*after addition of ammonium hydroxide
after addition of **acetic acid
***+ - few particles; ++ - more particles
DETD . . . to give the desired droplets. Then, the XAMA-7 crosslinking agent was added and the pH was decreased to 8-9 using **acetic acid**. The system was then allowed to crosslink at room temperature for 4 or 24 hours; then, the isopropanol dehydrating agent. . .

DETD . . . 212-150 um	--	--	69.7	68.8	
d. <150 um	--	--	30.3	7.0	

*1.2 .times. 10.sup.6

L37 ANSWER 9 OF 14 USPATFULL

ACCESSION NUMBER:	76:51293 USPATFULL
TITLE:	Bioerodible ocular device
INVENTOR(S):	Higuchi, Takeru, Lawrence, KS, United States Hussain, Anwar A., Lawrence, KS, United States Shell, John W., Los Altos, CA, United States
PATENT ASSIGNEE(S):	Alza Corporation, Palo Alto, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 3981303		19760921
APPLICATION INFO.:	US 1975-600793		19750731 (5)

RELATED APPLN. INFO.:	Division of Ser. No. US 1971-179129, filed on 9 Sep 1971, now abandoned
DOCUMENT TYPE:	Utility
FILE SEGMENT:	Granted
PRIMARY EXAMINER:	Medbery, Aldrich F.
LEGAL REPRESENTATIVE:	Ciotti, Thomas E., Sabatine, Paul L., Mandell, Edward L.
NUMBER OF CLAIMS:	22
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	7 Drawing Figure(s); 3 Drawing Page(s)
LINE COUNT:	1976

CAS INDEXING IS AVAILABLE FOR THIS PAT

```
CI    PMS, COM, MAN
PCT   Manual registration
LC    STN Files:   ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO,
        CA, CANCERLIT, CAPLUS, CASREACT, CHEMCATS, CHEMLIST, CIN, CSCHEM, CSNB,
        DDFU, DRUGU, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE,
        MSDS-OHS, NIOSHTIC, PROMT, RTECS*, TOXCENTER, USAN, USPATFULL
          (*File contains numerically searchable property data)
      Other Sources:   DSL**, TSCA**
          (**Enter CHEMLIST File for up-to-date regulatory information)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
             1296 REFERENCES IN FILE CA (1967 TO DATE)
                9 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
             1296 REFERENCES IN FILE CAPLUS (1967 TO DATE)


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     (FILE 'HOME' ENTERED AT 14:46:00 ON 03 MAY 2002)

     FILE 'REGISTRY' ENTERED AT 14:46:07 ON 03 MAY 2002
L1           284 S ALGINATE
L2             0 S SILICON GUM/CN
L3             0 S SILICA GUM/CN
L4             2 S SILIC? GUM
L5             2 S L4 OR (SILICON# GUM)

     FILE 'CAPLUS' ENTERED AT 15:04:28 ON 03 MAY 2002
L6           507 S L3 OR (SILICON# GUM)
L7             1 S DRUG (10W) L6
L8             6 S L6 AND TOPICAL
               S SODIUM TETRABORATE/CN

     FILE 'REGISTRY' ENTERED AT 15:08:20 ON 03 MAY 2002
L9             1 S SODIUM TETRABORATE/CN

     FILE 'CAPLUS' ENTERED AT 15:08:21 ON 03 MAY 2002
L10         3834 S L9

     FILE 'REGISTRY' ENTERED AT 15:08:24 ON 03 MAY 2002
L11            1 S SODIUM TETRABORATE/CN
L12            1 S AMMONIUM HYDROXIDE/CN
L13            1 S SODIUM ALGINATE/CN
L14            1 S SODIUM CARBONATE/CN
L15            1 S SODIUM BICARBONATE/CN
L16            1 S ACETIC ACID/CN
L17            1 S LACTIC ACID/CN
L18            1 S MALIC ACID/CN
L19            2 S GLUCONIC ACID/CN
L20            2 S ASCORBIC ACID/CN
L21            1 S GLYCERIN/CN
L22            1 S PROPYLENE GLYCOL/CN
L23            1 S ETHYLENE GLYCOL/CN
L24            1 S POLYETHYLENE GLYCOL/CN
L25            1 S POLYOXYETHYLENE SORBITAN MONOOLEATE/CN
L26            0 S POLYOXYETHYLENE SORBITAN TRIOOLEATE/CN
L27            0 S POLYOXYETHYLENE SORBITAN TRIOLEATE/CN
L28            1 S POLYOXYETHYLENE SORBITAN MONOPALMITATE/CN
```

=> d l25

L25 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS
RN 9005-65-6 REGISTRY
CN Sorbitan, mono-(9Z)-9-octadecenoate, poly(oxy-1,2-ethanediyl) derivs. (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Glycols, polyethylene, ether with sorbitan monooleate (8CI)
OTHER NAMES:
CN Alkamuls PSMO 20
CN Alkamuls T 80
CN Atlox 1087
CN Atlox 8916TF
CN Capmul POE-O
CN Cemerol T 80
CN Cemesol TW 1020
CN Crill 10
CN Crill 11
CN Crill S 10
CN Crillet 4
CN Crillet 4 Super
CN Crillet 41
CN Disponil SMO 120
CN Durfax 80
CN Ecoteric T 80
CN Emasol O 105R
CN Emsorb 6900
CN Emulson 10OM
CN Ethoxylated sorbitan monooleate
CN Ethylene oxide-sorbitan monooleate polymer
CN Eumulgin SMO 20
CN Flo Mo SMO 20
CN Glycosperse O 20
CN Glycosperse O 5
CN Hexaethylene glycol sorbitan monooleate
CN Hodag SVO 9
CN Ionet T 80
CN Ionet T 80C
CN Lamesorb SMO 20
CN MO 55F
CN Monitan
CN Montanox 80
CN Montanox 81VG
CN Montanox DF 80
CN Myvatex MSPS
CN Nikkol TO 10
CN Nikkol TO 106
CN Nikkol TO 10M
CN Nissan Nonion OT 221
CN Nonion OT 221
CN Olothorb
CN Polisorbac 60
CN Polyethoxylated sorbitan monooleate
CN Polyethylene glycol sorbitan ether monooleate
CN Polyethylene glycol sorbitan monooleate
CN Polyoxyethylated sorbitan monooleate
CN Polyoxyethylene monosorbitan monooleate
CN **Polyoxyethylene sorbitan monooleate**
ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT - Use FCN, FIDE, or ALL for DISPLAY

DR 8050-83-7, 9015-07-0, 9050-49-1, 9050-57-1, 1340-85-8, 51377-27-6, 61723-75-9, 37199-23-8, 37280-84-5, 141927-23-3, 178631-96-4, 209796-63-4, 361534-35-2
MF Unspecified
CI PMS, COM, MAN
PCT Manual registration, Polyether
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DIOGENES, DRUGU, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MRCK*, MSDS-OHS, NIOSHTIC, PDLCOM*, PIRA, PROMT, RTECS*, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: DSL**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
7595 REFERENCES IN FILE CA (1967 TO DATE)
44 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
7602 REFERENCES IN FILE CAPLUS (1967 TO DATE)

=> d 128

L28 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS
RN 9005-66-7 REGISTRY
CN Sorbitan, monohexadecanoate, poly(oxy-1,2-ethanediyl) derivs. (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Sorbitan, monopalmitate, polyoxyethylene derivs. (8CI)
OTHER NAMES:
CN Crill 7
CN Crillet 2
CN Durfax 60
CN Emsorb 6910
CN Emulgen TWP 120
CN Ethoxylated sorbitan monopalmitate
CN Glycosperse P 20
CN Lonzest SMP 20
CN Montanox 40
CN MP 55F
CN Nikkol TP 10
CN Nissan Nonion PT 221
CN Polyethylene glycol sorbitan monohexadecanoate
CN Polyethylene glycol sorbitan monopalmitate
CN Polyethylene glycol-sorbitan monopalmitate adduct
CN Polyethylene sorbitan monopalmitate
CN Polyoxyethylene sorbitan monohexadecanoate
CN **Polyoxyethylene sorbitan monopalmitate**
CN Polysorbate 40
CN Rheodol TW-P 120
CN Sorbimacrogol palmitate 300
CN Sorbitan monopalmitate polyethylene glycol ether
CN Sorbitan polyethoxy monopalmitate
CN Sorbon T 40
CN Tween 16:0
CN Tween 40
DR 9015-58-1, 1340-84-7, 118955-40-1
MF Unspecified

9 OF 16 USPATFULL

ACCESSION NUMBER:	2001:1817 USPATFULL
TITLE:	Method for improving the dispersion of redispersible polymer powders
INVENTOR(S):	Bodmeier, Roland, Ravenberg 18, 14163 Berlin, Germany, Federal Republic of McGinity, James W., 4209 Dunning La., Austin, TX, United States 78746

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6169130	B1	20010102	
APPLICATION INFO.:	US 1999-316815		19990521	(9)

	NUMBER	DATE
PRIORITY INFORMATION:	DE 1998-19824650	19980524

DOCUMENT TYPE:	Utility
FILE SEGMENT:	Granted
PRIMARY EXAMINER:	Sanders, Kriellion
LEGAL REPRESENTATIVE:	Matos, RickInnovar, L.L.C.
NUMBER OF CLAIMS:	20
EXEMPLARY CLAIM:	1

ACCESSION NUMBER:	2002:88006 USPATFULL
TITLE:	Bioadhesive hot-melt extruded film for topical and mucosal adhesion applications and drug delivery and process for preparation thereof
INVENTOR(S):	Repka, Michael A., 700 Oak Hill Dr., Oxford, MS, United States 38655 Repka, Staci L., 700 Oak Hill Dr., Oxford, MS, United States 38655 McGinity, James W., 4209 Dunning La., Austin, TX, United States 78746

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6375963	B1	20020423	
APPLICATION INFO.:	US 2000-594294		20000615	(9)

	NUMBER	DATE	
PRIORITY INFORMATION:	US 1999-139411P	19990616	(60)

DOCUMENT TYPE:	Utility
FILE SEGMENT:	GRANTED
PRIMARY EXAMINER:	Page, Thurman K.
ASSISTANT EXAMINER:	Ware, Todd D
LEGAL REPRESENTATIVE:	Matos, Rick, Innovar, L.L.C.
NUMBER OF CLAIMS:	36
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	1 Drawing Figure(s); 1 Drawing

L10 ANSWER 2 OF 38 USPATFULL
ACCESSION NUMBER: 2001:102501 USPATFULL
TITLE: Surface-crosslinking process for water-absorbent resin
INVENTOR(S): Ishizaki, Kunihiko, Suita, Japan
Kanto, Teruyuki, Himeji, Japan
Sakamoto, Shigeru, Himeji, Japan
Harada, Nobuyuki, Suita, Japan
Hitomi, Kazuhisa, Himeji, Japan
PATENT ASSIGNEE(S): Nippon Shokubai Co., Ltd., Osaka, Japan (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6254990	B1	20010703	
APPLICATION INFO.:	US 1999-250477		19990214	(9)

	NUMBER	DATE
PRIORITY INFORMATION:	JP 1998-36197	19980218

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Wilson, Donald R.
NUMBER OF CLAIMS: 17
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 3 Drawing Figure(s); 3 Drawing Page(s)
LINE COUNT: 2030
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM . . . In addition, when the water-absorbent resin is formed into scales, its absorption speed is improved, but is still insufficient because **gel**-blocking is induced, and further, forming the water-absorbent resin into scales is uneconomical in that the resultant water-absorbent resin is necessarily. . .
SUMM . . . set forth in JP-A-58-042602). Furthermore, there is also a known art in which a crosslinking agent is added to a **hydrogel**, and the resultant mixture is dried and then divided finely and then

L10 ANSWER 5 OF 38 USPATFULL

ACCESSION NUMBER:	2001:22318 USPATFULL
TITLE:	Water-absorbent agent and method for manufacturing the same
INVENTOR(S):	Yanase, Toru, Ibo-gun, Japan Kimura, Kazuki, Himeji, Japan Fujino, Shin-ichi, Himeji, Japan Nagasuna, Kinya, Himeji, Japan Ishizaki, Kunihiko, Suita, Japan Fujimaru, Hirotama, Himeji, Japan Harada, Nobuyuki, Suita, Japan
PATENT ASSIGNEE(S):	Nippon Shokubai Co., Ltd., Osaka, Japan (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6187872	B1	20010213	
	WO 9805420		19980212	
APPLICATION INFO.:	US 1998-51313		19980406	(9)
	WO 1997-JP2706		19970805	
			19980406	PCT 371 date
			19980406	PCT 102(e) date

	NUMBER	DATE
PRIORITY INFORMATION:	JP 1996-208622	19960807

DOCUMENT TYPE:	Utility
FILE SEGMENT:	Granted
PRIMARY EXAMINER:	Wu, David W.
ASSISTANT EXAMINER:	Zalukaeva, Tanya
LEGAL REPRESENTATIVE:	Nixon & Vanderhye
NUMBER OF CLAIMS:	37
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	4 Drawing Figure(s); 3 Drawing Page(s)
LINE COUNT:	3083

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A **hydrogel** polymer obtained by polymerizing a monomer component including acrylic acid (salt) is post-neutralized so that each of polymer particles derived from a polymer produced by neutralizing the **hydrogel** polymer has an allowable neutralization ratio. The polymer as obtained by neutralizing the **hydrogel** polymer is reacted with a crosslinking agent reactive to a functional group of the polymer. The allowable neutralization ratio, for. . . of water soluble component is lower compared with the conventional water-absorbent agent and a change in pH of a swollen **gel** is small.

SUMM . . . be manifested upon contact with aqueous liquids such as body fluids, (b) liquid permeability, (c) high strength exhibited by a **gel** swollen with liquid, and (d) an ability to aspirate water from a substrate impregnated with aqueous liquid.

SUMM . . . to one another such that, for example, as absorbency of water-absorbent resin increases, such properties as the liquid permeability, the **gel** strength, and the absorbing rate decrease. In order to improve a balance of the various water-absorbent properties of the water-absorbent. . .

SUMM . . . which have not been neutralized or have been neutralized at a relatively low neutralization ratio within a predetermined range,

resulting **hydrogel** polymer is neutralized as required. For example, the method (I) is adopted as the manufacturing method of water-absorbent resin disclosed. . .

SUMM . . . of a vinyl crosslinking agent, the acrylic acid thus polymerized is neutralized with alkali metals, and resulting water containing neutralized **gel** is further crosslinked by divalent metal ions (U.S. Pat. No. 4,295,987), (m) a method in which an alkali metal containing compound is added to a **hydrogel** polymer which has been prepared by polymerizing monomers containing a free acid group such as carboxylic acid, and at least 50 mole percent of the acid group of the **hydrogel** polymer are neutralized (U.S. Pat. No. 4,654,039), (n) a method in which an alkali metal containing compound is added to a **hydrogel** polymer which has been prepared by polymerizing a monomer containing a free acid group such as carboxylic acid using a copolymerizable crosslinking agent, and 50 mole percent to 90 mole percent of the acid group of the **hydrogel** polymer are neutralized, (o) a method in which an alkali metal containing compound is added to a **hydrogel** polymer which has been prepared by polymerizing a monomer containing an acid group such as carboxylic acid, and after neutralizing 50 mole percent to 90 mole percent of the acid group of the **hydrogel** polymer, the **hydrogel** polymer is crosslinked to a compound having at least two or more reactive groups which can undergo reaction with the acid group of the **hydrogel** polymer, and/or an alkali metal base of the acid group (Japanese Unexamined Patent Application No. 103606/1989 (Tokukaihei 1-103606), and Japanese. . . ppm, resulting polyacrylic acid is neutralized at a

ANSWER 21 OF 38 USPATFULL

ACCESSION NUMBER:	89:57687 USPATFULL
TITLE:	Article for permanent structure alteration of hair
INVENTOR(S):	Bires, Carmen D., Long Valley, NJ, United States Helioff, Michael W., Westfield, NJ, United States Chaudhuri, Ratan K., Butler, NJ, United States
PATENT ASSIGNEE(S):	GAF Corporation, Wayne, NJ, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 4848377		19890718	
APPLICATION INFO.:	US 1987-105783		19871008	(7)
DISCLAIMER DATE:	20051227			
DOCUMENT TYPE:	Utility			
FILE SEGMENT:	Granted			
PRIMARY EXAMINER:	Mancene, Gene			
ASSISTANT EXAMINER:	Lepiane, Adriene J.			
LEGAL REPRESENTATIVE:	Maue, Marilyn J., Ward, Joshua J.			
NUMBER OF CLAIMS:	17			
EXEMPLARY CLAIM:	1			
LINE COUNT:	678			

SUMM . . . include pads, swatches or rollers composed of paper, woven or non-woven material in the form of a fabric, plastic, felt, **sponge**, gauze, or blotter which includes both mono- and poly-ply laminated materials such as the laminations employed for diapers, etc. Also, . . . smooth surface or be crimped or creped to attain additional absorbent properties. Particularly suitable is microsponge, preferably closed pore non-retriculated **sponge** having from about 5 to about 150 pores/inch, most preferably from about 40 to about 120 pores/inch.

SUMM . . . or impregnated on one or both sides of its surface or be completely saturated with a suitable hair altering solution **gel** or paste, as described in U.S. Pat. No. 4,206,196, incorporated herein by reference.

SUMM . . . in the form of a winding rod, e.g., as a tubular spongy material impregnated with the waving lotion. Further, such **sponge** rollers may be secured in rolled position by including on their surface a plurality of interlocking filaments. Such a filamented. . .

SUMM . . . formulations. As the term "lotion" is used herein, it is to be understood that this term includes a cream, a **gel**, an emulsion or a watery liquid.

SUMM . . . 0.03

Potassium iodide	0.60
Water	97.34

BISULFITE WAVING FORMULATION

Ingredients	% By Weight
Water	55.55
Ammonium bisulfite	22.00
Hydroxyethyl cellulose	2.50
Urea	10.00
Isopropyl alcohol	5.00
Disodium phosphate	1.14
Citric acid	0.46
Ammonium hydroxide	1.10
Chelating agent	0.05

Fragrance	0.20
Surfactant	2.00

and

Ingredients	% By Weight
Sodium bisulfite	6.46
Sodium borate	4.10
Sodium carbonate	4.10
Monoethanolamine	4.92
Diethanolamine	4.92
Wetting agent	1.00
Water q.s. to	100.00

SUMM . . . or both surfaces, optionally dried and then packaged in a moisture proof container. The latter procedure is particularly useful for **gel**, cream or pasty hair straightening lotions. If desired, several coatings of the solution can be applied to the surface of. . .

SUMM . . . of the above techniques or other means of coating can be used to apply reducing lotion to a monoply wrapping **sponge**, gauze or between or on the plies of a multiply material composed of paper, plastic, felt or microsponge.

DETD A second test subject was tested with Zotos Design Freedom permanent waving lotion (5 fluid ounces) using **sponge** swatches and the procedure described in Example 1 for impregnation. The hair of test subject was not previously processed, had. . .

DETD . . . treatment, the hair was sectioned into 25 parts and the distal ends of each part was wrapped in an impregnated **sponge** swatch end paper and rolled on a permanent hair setting rod of about 1/4 inch diameter and 5 inch length,. . .

CLM What is claimed is:

2. The article of claim 1 wherein the wrapping is **sponge** having a thickness of from about 1/32 to about 1 inch thickness and having from about 5 to about 150. . .

5. The aritcle of claim 4 wherein the microsponge is in the form of a swatch or **pad** having a dimension of about 4.times.3-6 inches and between about 40 and about 120 pores/inch.

17. The article of claim 12 wherein said flexible hair wrapping material is a **sponge** having a thickness of from about 1/32 to about 1 inch.

```
L1   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2002 ACS
RN   1330-43-4  REGISTRY
CN   Boron sodium oxide (B4Na2O7) (9CI)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   Boric acid (H2B4O7), disodium salt (8CI)
CN   Sodium tetraborate (Na2B4O7) (7CI)
OTHER NAMES:
CN   Anhydrous borax
CN   Borax glass
CN   Disodium tetraborate
CN   FR 28
CN   Fused Borax
CN   Rasorite 65
CN   Sodium biborate
CN   Sodium borate
CN   Sodium boron oxide (Na2B4O7)
CN   Sodium tetraborate
DR   12045-54-4, 12589-17-2, 13764-83-5, 163701-93-7, 1332-28-1, 19223-62-2,
     115372-65-1, 136349-33-2, 37199-25-0
MF   B4 Na2 O7
CI   COM, MAN
LC   STN Files:   AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA,
       CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN,
       CSCHEM, CSNB, DETHERM*, DIOGENES, EMBASE, HSDB*, IFICDB, IFIPAT,
IFIUDB,
       MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PDLCOM*, PIRA, PROMT, RTECS*,
       TOXCENTER, TULSA, ULIDAT, USAN, USPAT2, USPATFULL
         (*File contains numerically searchable property data)
     Other Sources:   DSL**, EINECS**, TSCA**
         (**Enter CHEMLIST File for up-to-date regulatory information)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
            3808 REFERENCES IN FILE CA (1967 TO DATE)
              32 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
            3810 REFERENCES IN FILE CAPLUS (1967 TO DATE)
               1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)


=> d l2

L2   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2002 ACS
RN   1336-21-6  REGISTRY
CN   Ammonium hydroxide ((NH4)(OH)) (9CI)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   Ammonium hydroxide (8CI)
OTHER NAMES:
CN   19: PN: WO0175077 SEQID: 20 claimed sequence
CN   Ammonia water
CN   Ammonia, aqua
CN   Ammonia, monohydrate
CN   Aqua ammonia
CN   SX 1
CN   SX 1 (ammonia water)
DR   132103-60-7, 125888-87-1, 16393-49-0
MF   H5 N O
CI   COM
LC   STN Files:   AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA,
       CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX,
       CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DETHERM*, DIPPR*, DRUGU, EMBASE,
```

ENCOMPLIT, ENCOMPLIT2, ENCOMPPAT, ENCOMPPAT2, GMELIN*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MSDS-OHS, NIOSHTIC, PDLCOM*, PIRA, PROMT, RTECS*, TOXCENTER, TULSA, USPAT2, USPATFULL, VETU, VTB
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)

H_4N-OH

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

10523 REFERENCES IN FILE CA (1967 TO DATE)
154 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
10530 REFERENCES IN FILE CAPLUS (1967 TO DATE)

	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Errors
1	IS&R	L1	9811	((424/400-401) or (424/404) or (424/405-407) or (424/414-417) or (424/430-437) or (424/443-449)).CCLS.	USPAT; US-PGPUB	2002/05/03 15:26			0
2	BRS	L2	36609	algin$4	USPAT; US-PGPUB	2002/05/03 15:27			0
3	BRS	L3	1301	1 and 2	USPAT; US-PGPUB	2002/05/03 15:27			0
4	BRS	L4	3964	tetraborate	USPAT; US-PGPUB	2002/05/03 15:27			0
5	BRS	L5	41293	ammonium adj hydroxide	USPAT; US-PGPUB	2002/05/03 15:27			0
6	BRS	L6	2	nh4 adj oh	USPAT; US-PGPUB	2002/05/03 15:28			0
7	BRS	L7	268	nh4oh	USPAT; US-PGPUB	2002/05/03 15:28			0
8	BRS	L8	94705	nh$4	USPAT; US-PGPUB	2002/05/03 15:29			0
9	BRS	L9	2	3 and 4	USPAT; US-PGPUB	2002/05/03 15:29			0

	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Errors
10	BRS	L10	45	3 and 5	USPAT; US-PGPUB	2002/05/03 15:29			0
11	BRS	L11	0	3 and 6	USPAT; US-PGPUB	2002/05/03 15:29			0
12	BRS	L12	0	3 and 7	USPAT; US-PGPUB	2002/05/03 15:29			0
13	BRS	L13	99	3 and 8	USPAT; US-PGPUB	2002/05/03 15:30			0
14	BRS	L14	170201	sponge or foam	USPAT; US-PGPUB	2002/05/03 15:30			0
15	BRS	L15	607	2 same 14	USPAT; US-PGPUB	2002/05/03 15:30			0
16	BRS	L16	5	15 and 13	USPAT; US-PGPUB	2002/05/03 15:30			0
17	BRS	L17	11	10 and 14	USPAT; US-PGPUB	2002/05/03 15:31			0
18	BRS	L18	17	16 or 17 or 9	USPAT; US-PGPUB	2002/05/03 15:37			0

	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Errors
19	IS&R	L19	5	(("6214331") or ("6207696") or ("5158766") or ("3948881") or ("5133803")).PN.	USPAT; US-PGPUB	2002/05/03 15:40			0
20	BRS	L20	7117	5 and 14	USPAT; US-PGPUB	2002/05/03 15:40			0
21	BRS	L21	2	19 and 14	USPAT; US-PGPUB	2002/05/03 15:40			0

US005718916A

United States Patent [19]

Scherr

[11] Patent Number: 5,718,916

[45] Date of Patent: Feb. 17, 1998

[54] **ALGINATE FOAM PRODUCTS**

[76] Inventor: George H. Scherr, P.O. Box 134, Park Forest, Ill. 60466

[21] Appl. No.: 792,374

[22] Filed: Feb. 3, 1997

[51] Int. Cl.[6] A61L 15/00

[52] U.S. Cl. 424/445; 424/400; 424/484

[58] Field of Search ..... 424/44, 445, 443, 424/619, 715, 722, 43, DIG. 13, 484, 400; 604/85, 304; 523/111, 113

[56] References Cited

U.S. PATENT DOCUMENTS

3,653,383	4/1972	Wise	128/296
4,948,575	8/1990	Cole et al.	424/44
5,089,606	2/1992	Cole et al.	536/54
5,409,703	4/1995	McAnalley et al.	424/435
5,470,576	11/1995	Patel	424/445

Primary Examiner—Thurman K. Page

Assistant Examiner—Kathryne E. Shelborne

[57] **ABSTRACT**

A composition sodium alginate which is capable of being formed into an insoluble alginate salt in a mold or dish which insoluble alginate salt may be frozen and lyophilized resulting in an alginate foam product which has utility in wound management as a dressing, in surgical, and implant procedures. The insoluble alginate salt thus formed may also be prepared as a coercive mixture or covalent-link mixture with insolubilizing chemical agents which thus provide a product having utility as a medical dressing, in surgical, and implant procedures, which can retain their integrity in or on tissues over extended periods of time and a method of making the same.

22 Claims, No Drawings

ALGINATE FOAM PRODUCTS

The present invention relates to novel alginate compositions and methods of making same, which can be utilized in the medical and veterinary fields. More specifically, the invention relates to novel compositions of alginate which can be prepared in the form of a sponge-like or foam product which, according to the composition, may be utilized in the preparation of various bandages or surgical products.

Alginates are polysaccharide-like compounds extracted from certain sea weeds and have been described in great detail in numerous reports, literature, and patents (Kelco Algin, 2nd Ed., pgs 1–50, Kelco Co., Chicago Ill. 60606; Alginates in Pharmaceuticals and Cosmetics, Alginate Industries, Ltd., London W.C.2, Great Britain; Properties of Alginates, R. H. McDowell, Alginate Industries, Ltd., London, England, 1955; Alginates and Alginate Fibers in Clinical Practice, George H. Scherr, Wounds, Vol. 4, No. 2, 1992; U.S. Pat. Nos. 1,778,688; 1,814,981; 1,814,986; 2,477,861; and others.

One of the salient attributes of alginates is their ability to form gels when they react with certain polyvalant cations. Thus sodium alginate solutions which are soluble in water and other aqueous media will form gels when reacted with certain polyvalant ions which include calcium, zinc, aluminum, copper, and silver. The formation of alginate gels have been described in the literature and in patents (Kelco, ibid; U.S. Pat. Nos. 2,420,308; 3,349,079 and 3,386,921). The polyvalant ion-alginate gels so formed, such as calcium alginate, are insoluble in water but will dissolve in solutions of sodium salts of organic acids such as sodium hexametaphosphate, sodium glycero-phosphate, or sodium citrate.

The present invention utilizes alginates which are precipitated in a solution of a polyvalant ion such as calcium or zinc resulting in an aqueous insoluble product that could have utility in the fields of medicine, dentistry, or surgery when formed into bandages, dressings, or implants.

A study describing the use of absorbable alginate fiber dressings in the use of surgery was made by Blaine (George Blaine, Experimental Observations on Absorbable Alginate Products in Surgery, Annals of Surgery, January, 1947; pp 102–114). Alginate fibers and films were shown by Blaine to enhance the rate of healing in experimental animals as contrasted with controls.

Fairbairn and Whittet (J. W. Fairbairn and T. D. Whittet, Absorbable Haemostatics: Their Uses and Identification, The Pharmaceutical Journal, Feb. 28, 1948; pp 149–150), and Oliver & Blaine (British J. of Surgery, 37:1–4, 1950), reported that alginate fibers when used as absorbable hemostatic agents had significant advantages over oxidized cellulose in that oxidized cellulose inactivated penicillin whereas alginate did not and also that oxidized cellulose could not be sterilized by heat whereas alginate fibers could readily be sterilized by heat without their being significantly altered in physical and chemical characteristics.

Additional reports of the hemostatic properties of alginates have been made by Gosset (Texte de la communication faite le 16 mars 1949, a l'Academie de Chirurgie de Paris, Hopitaux de Paris; Twenty-Five Dental Cases Treated With Absorbable Alginate Wool, J. F. S. Rumble, British Dental Journal, Vol. LXXXVI, No. 8, 1949; A New and Effective Haemostatic Agent, Clifton A. H. Smith, Science, Vol. 103, No. 2681, Pg 634, 1946; Results With Alginate Materials in the Casualty Department of the Croydon General Hospital, Clarice Bray, Croydon General Hospital, Croydon, U.K.; Oral Use of Absorbable Alginate Derivatives to Arrest and Prevent Postextraction Hemorrhage, L. J. Allen, Oral Surgery, Oral Medicine, and Oral Pathology, Vol. 6, No. 2, pp 336–338, 1953;New Surgical Absorbable Hemostatic Agent, E. S. Hurwitt, et al., American Journal of Surgery, Vol. 100, 1960.

U.S. Pat. No. 3,853,383 describes a water-absorbant and water-disintegrative algin sponge prepared from alginic acid which may be utilized in medical or biological applications in which the alginate composition is quick frozen and then lyophylized resulting in an open cell porous alginate sponge product. The U.S. Pat. No. 3,853,383 utilizes a complex chemical procedure in which alginic acid is converted in part to calcium alginate and in part to sodium alginate after which all of this material has to be dried and pressed to remove alcohol and water and then milled in order to achieve a certain mesh size and the milled powder is then dissolved in water and blended at very high speed after which it is placed in a tray and lyophilized. (Although the U.S. Pat. No. 3,653,383 characterizes the mixture of calcium alginate and sodium alginate as being soluble (dissolved) in water prior to its being blended, calcium alginate is insoluble in water and it is not clear how such solution takes place as claimed in this patent. Although the abstract of the patent and the summary of the invention all set forth that the algin sponge so prepared is both water absorbent and water disintegrative, it is noted that all of the claims indicate that the calcium alginate component of the sponge is water insoluble; consequently a water insoluble alginate would not be expected to disintegrate in water).

U.S. Pat. No. 4,948,575 describes an alginate hydrogel foam wound dressing in which the sodium alginate solution, calcium containing insolubilizing solution, and foam-making chemicals are used in situ. Thus, all the chemical reactions take place at the site of and in the wound and lacks the capability of being stored as a dressing in a sterile form and made immediately available for use when required.

Alginates can be fabricated in a wide variety of compositions and are isolated from various species of seaweeds. It is noteworthy that the various alginates are composed of mannuronic acid and guluronic acid in various proportions. It has been shown that the relative proportion of mannuronic acid and guluronic acid may vary depending upon the species of seaweed from which they are extracted. Thus, the mannuronic acid content of alginate isolated from *Macrocystis pyrifera* is approximately 61% to 39% for guluronic acid whereas the mannuronic acid content of alginate isolated from *Laminaria hyperborea* is 31% to 69% for guluronic acid. Those alginates that have a high percentage of guluronic acid form rigid or brittle gels, whereas the alginates isolated from *Macrocystis pyrifera* contain a higher percentage of mannuronic acid and form elastic gels which can be deformed.

It is well known that the addition of calcium ions or in fact other earth metal ions such as zinc, aluminum, silver, or copper will precipitate alginate in the form of the metal ion alginate aqueous insoluble form. It is frequently desirable to prepare calcium alginate gels in certain physical forms. In order to achieve that, the precipitate of the calcium or other earth metal ion insoluble alginate has to be sequestered in order to permit the solution to be poured into a mold or a form and gelation take place after a suitable period of time so that the insoluble alginate gel will retain the form of the mold into which it is poured. Consequently, sequestering agents may be utilized such as ethylene, diamine, tetra-acetic acid (EDTA) or sodium citrate (citric acid, trisodium salt dihydrate) in which the sequestering agent retards the precipitation of the insoluble metal ion alginate gel for a

period of time that permits the sodium alginate and Ca^{++} ion containing solution to be poured into a mold. Another method which has been utilized is to use an insoluble calcium salt such as calcium carbonate and by adding such an insoluble calcium salt to a solution of sodium alginate, which is then poured into a gel, the calcium ion reacts very slowly with the alginate moiety and consequently, precipitation of the calcium alginate gel is detained for an extended period of time, prior to gelation taking place in a suitable mold or container.

Alginate products when prepared as dressings, bandages, or implants, may require varying rates of disintegration in tissues depending upon the purpose for which they are to be used. It is one of the aspects of this invention that alginate products may be prepared having varying rates of disintegration in or on tissues depending upon specific needs. For example, bandages may be utilized as hemostats or dressings to cover exudating or nonexudating wounds or burns. Such dressings should retain their integrity for at least one to two weeks during which period the dressing may be lifted to examine the progress of a wound and, when desired, the dressing can be readily removed and a fresh dressing replaced thereon. Were the dressing to disintegrate very quickly in or on an exudating wound, then removal of the alginate dressing, which frequently disintegrates into a gelatinous amorphous entity, would be extremely difficult. On the other hand, were the alginate product formed for utilization as an implant which would have to retain its integrity for a few months or more, then it would be necessary to ensure that the product did not disintegrate in situ prior to the required time of its action. The capability inherent in our invention to alter the rates of alginate disintegration may principally be achieved by two methods:

Method A

The alginate composition is mixed with reagents and/or polymers which become coercive to the alginate molecule when the composition is so introduced into a calcium chloride solution, resulting in a precipitate and so entrapping the total composition. If the reagents or polymers other than that of alginate which are used have a high resistance to enzymatic and/or aqueous deterioration in tissues, then the time of retention of the integrity of the alginate product so prepared will be prolonged. Whereas, if the proportion of such an aqueous insoluble or enzyme-resistant polymer which becomes an integral micelle in the polymer network of the calcium alginate gel is thus reduced, then the time of dissolution of the alginate composition is shortened.

Method B

A solution of sodium alginate is mixed with calcium ions which are concomitantly mixed with a cross-linking agent to the sodium alginate where the cross-linking agent is resistant to aqueous and/or enzymatic deterioration in tissues. Thus for example, by altering the proportion of the calcium alginate left free as an insoluble gel and the calcium alginate which has been cross-linked to an insoluble moiety thus rendering it less susceptible to deterioration in aqueous tissues and/or resistant to enzymatic breakdown in tissues, then by thus adjusting the proportions of these two compounds, the rate of dissolution of this molecular complex could thereby be altered. The alteration of the rate of dissolution of such an alginate-cross-linked complex would result in an alteration in the rate of dissolution of the alginate dressing or implant in or on tissues.

Having set forth the tenets of the invention contained herein, the following non-limiting examples illustrate various compositions that are inherent in our invention:

EXAMPLE 1

Twenty ml of a 3.0% solution of Kelco sodium alginate XL-F is added to 12 ml of 2.0% sodium citrate as sodium citrate $0.6H_2O$.

The mixture is stirred and to it is added 0.5 ml of glycerin and 0.15 ml of surface active agent encoded L64, polyal BASF by Wyandotte Corp. After the composition has been stirred, 6 ml of 2% calcium chloride as calcium chloride $0.2H_2O$ is added slowly with vigorous stirring and when thoroughly mixed, the total composition is poured into a plate, dish or similar container. The liquid mixture of sodium alginate will gel in approximately 30 to 60 seconds after which time the plate or dish containing the gelled calcium alginate mixture is then quickly frozen, either in a freezer, dry ice chest, or liquid nitrogen.

The sodium citrate acts as a sequestering agent and delays immediate precipitation of the calcium alginate which otherwise would result in an incoherent number of insoluble calcium alginate globules.

After the dish containing the alginate mixture has been suitably frozen, it is inserted into a vacuum chamber, during which time lyophilization proceeds under vacuum until the moisture has been withdrawn. The resulting composition is a microporous dressing having excellent uniformity and being composed of calcium alginate.

EXAMPLE 2

Add 37.5 ml of a 3.0% solution of Kelco sodium alginate XL-F to 15.0 ml of a 2.0% solution of sodium citrate as sodium citrate $0.6H_2O$.

The mixture is stirred and to it is added 150 mg of porcine collagen dispersed as a colloidal dispersion in 10 ml of solution. To this mixture is added 0.5 ml of glycerin and 0.15 ml of the L-64 surface active agent. After the composition has been stirreds 7.0 ml of 2% calcium chloride as calcium chloride $0.2H_2O$ is added slowly with vigorous stirring, and when thoroughly mixed, the total composition is poured into a plate, dish, or similar container. After gelation has occured, the dish containing the gelled calcium alginate-collagen mixture is then quickly frozen either in a freezer, ice chest or liquid nitrogen.

As in Example 1, the sodium citrate acts as a sequestering agent and delays immediate precipitation of calcium alginate.

The dish containing the mixture which has been frozen, is then inserted into a vacuum chamber and lyophilized as described in Example 1.

This composition couples the unique advantages of calcium alginate as well as collagen for use in dressings that would act as a hemostat and in the reduction of bleeding time as well as forming a hydrocolloidal gel which has been shown to enhance the healing process when such dressings are utilized.

EXAMPLE 3

The zinc salt of bacitracin, having a concentration of 67 IU/mg, is added in an amount of 230 mg to 10 ml of deionized water. Neomycin sulphate powder assaying as 704 mog neomycin/mg of material is added to 10 ml of deionized water in an amount of 135 mg. Polymyxin B sulphate containing 8547 units of polymyxin B/mg of powder is added to 10 ml of deionized water in an amount of 22.6 mg.

The three separate solutions are stirred until all of the antibiotics have been dissolved and then they are mixed, to

form a total of 30 ml of solution. To the antibiotic mixture is slowly added 30.0 ml of 5.0% sodium alginate XL-F and 0.5 ml of glycerin as well as 0.15 ml of L64 surface active agent.

The total solution is initially slowly stirred and then vigorously mixed while adding drop wise a mixture of 3.0 ml of a 2.0% solution of calcium chloride as calcium chloride $0.2H_2O$ and 12.0 ml of 2.0% sodium citrate as sodium citrate $0.6H_2O$.

The total solution is then poured into a dish, and after gelation has occurred, the dish is quick frozen either in a freezer, dry ice chest, or liquid nitrogen following which lyophilization takes place as described in Example 1 above.

EXAMPLE 4

Sodium alginate having a viscosity in aqueous solution of 170 centepoise at 2.0% concentration is dissolved in 100 ml of deionized or distilled water at a concentration of 2.0%. This solution also contains the following ingredients at final concentrations as indicated:

A surface active agent-dioctyl derivative of succinic acid (aerosol OT-B)	50 mg
Vegetable oil (Coconut oil)	0.15 ml
Glycerin	0.2 ml
A surface active agent (Tween 80)	0.1 ml
Polyvinyl pyrolidine (PVP, 360,000 M.W.)	50 mg

This mixture is stirred with a magnetic stirrer until all of the reagents have been mixed.

To a solution of 12.0 ml of 2.5% calcium chloride as calcium chloride $0.2H_2O$ is added 2.0 grams of sodium citrate as sodium citrate $0.6H_2O$. The calcium chloride-sodium citrate solution is thoroughly mixed until all ingredients are dissolved and this solution is added to the alginate mixture prepared above with vigorous stirring and immediately following, the total composition is poured into a dish or plate, frozen and lyophilized as set forth in Example 1 above.

EXAMPLE 5

The sodium alginate solution described in Example 4 above is prepared and this alginate solution also now contains the following at the final concentrations shown:

A surface active agent-dioctyl derivative of succinic acid (aerosol OT-B)	150 mg
Glycerin	3.0 ml
A surface active agent (Tween 80)	0.1 ml
A carboxylated styrene butadiene copolymer latex (Encoded 68-412 by the Reichhold Chemical Co.)	0.5 ml

Twenty ml of a 3.0% solution of Kelco sodium alginate XL-F is added to 12 ml of 2.0% sodium citrate as sodium citrate $0.6H_2O$.

The sodium citrate acts as a sequestering agent and delays immediate precipiation of calcium alginate which otherwise would result in an incoherent number of insoluble calcium alginate globules.

The mixture is stirred and to it is added 0.5 ml of glycerin and 0.15 ml of L64 surface active agent. After the above composition has been stirred, slowly add a mixture containing 6 ml of 2% calcium chloride as calcium chloride $0.2H_2O$ and 12 ml of 2.0% sodium citrate as sodium citrate $0.6H_2O$ with vigorous stirring and when thoroughly mixed, the total composition is poured into a plate, dish or similar container. The mixture containing calcium alginate will gel in approximately 30 to 60 seconds, after which time the plate or dish containing the gelled calcium alginate mixture is then quickly frozen, either in a freezer, dry ice chest or liquid nitrogen following which lyophilization takes place as described in Example 1 above.

EXAMPLE 6

Sodium alginate having a viscosity as described in Example 4 is dissolved in 100 ml of deionized or distilled water to a final concentration of 2.0%. This solution also contains the following ingredients at final concentrations as indicated:

A surface active agent-dioctyl derivative of succinic acid (aerosol OT-B)	150 mg
Glycerin	3.0 ml
A surface active agent (Tween 80)	0.1 ml
A carboxylated styrene butadiene copolymer latex (encoded 68-412 by the Reichhold Chemical Co.)	0.5 ml
A melamine-formaldehyde condensate (Encoded M-3 by American Cyanamid Co.)	5.0 ml

The mixture is stirred as described in Example 4.

To a solution of 20 ml of 2.5% calcium chloride as calcium chloride $0.2H_2O$ is added 1.0 gram of sodium citrate as sodium citrate $0.6H_2O$. The calcium chloride-sodium citrate solution is thoroughly mixed until the ingredients are dissolved and to it is added an amount of ammonium chloride to yield a final concentration of 5.0% of ammonium chloride. The calcium chloride-sodium citrate-ammonium chloride solution is added to the alginate mixture prepared above with vigorous mixing until a homogenous dispersion occurs and it is immediately poured into a dish, or plate, frozen, and lyophilized as set forth in Example 1 above.

EXAMPLE 7

A solution of sodium alginate is prepared as described in Example 4 above. This solution also contains the following ingredients at final concentrations as indicated:

Glycerin	3.0 ml
A surface active agent (Tween 80)	.75 ml
A carboxylated styrene butadiene copolymer latex (Encoded 68-412 by the Reichhold Chemical Co.)	0.5 ml
A melamine-formaldehyde crosslinking agent (Encoded M-3 by American Cyanamid Co.)	5.0 ml
Alkanolamine hydrochloride (20%)	1.0 ml

To a solution of 20 ml of 2.5% calcium chloride as calcium chloride $0.2H_2O$ is added 1.0 gram of sodium citrate as sodium citrate $0.6H_2O$. The calcium chloride-sodium citrate solution is throughly mixed until all ingredients are dissolved and this solution is added to the alginate mixture prepared above with vigorous stirring and immediately

following, the total composition is poured into a dish or plate, frozen and lyophilized as set forth in Example 1 above.

EXAMPLE 8

Sodium alginate having a viscosity in aqueous solution of 170 centepoise at 2.0% concentration is dissolved in 100 ml of deionized or distilled water at a final concentration of 2.0%. This solution also contains the following ingredients at final concentrations as indicated:

Glycerin	3.0 ml
A surface active agent (Tween 80)	.75 ml
A carboxylated styrene butadiene copolymer latex (Encoded 40-438 by the Reichhold Chemical Co.)	1.0 ml
A melamine-formaldehyde crosslinking agent (Encoded 3730 by American Cyanamid Co.)	0.2 ml
Coconut oil	0.2 ml
A surface active agent (Encoded Pluronic L64 (Polyal BASF by Wyandotte Corp.)	0.2 ml
Polyethylene glycol 5% aqueous solution	1.0 ml
An anionic water dispersed micro particle wax dispersion (labeled MICHEM Lube 270 by Michelman, Inc.)	1.0 ml

To a solution of 20 ml of 2.5% calcium chloride as calcium chloride $0.2H_2O$ is added 1.0 gram of sodium citrate as sodium citrate $0.6H_2O$. The calcium chloride-sodium citrate solution is thoroughly mixed until the ingredients are dissolved and this solution is added to the alginate mixture prepared above with vigorous stirring and immediately following, the total composition is poured into a dish or plate, frozen and lyophilized as set forth in Example 1 above.

EXAMPLE 9

Sodium alginate having a viscosity in aqueous solution of 170 centepoise at 2.0% concentration is dissolved in 100 ml of deionized or distilled water at a final concentration of 2.0%. This solution also contains the following ingredients at final concentrations as indicated:

Glycerin	3.0 ml
A surface active agent (Tween 80)	.75 ml
A surface active agent-dioctyl derivative of succinic acid (aerosol OT-B)	50 mg
Coconut oil	0.8 ml
An anionic water dispersed micro particle wax dispersion (labeled MICHEM Lube 270 by Michelman, Inc.	5.0 ml
Polyvinyl alcohol (PVA 124,000 M.W.)	0.2%

To a solution of 20 ml of 2.5% calcium chloride as calcium chloride $0.2H_2O$ is added 1.0 gram of sodium citrate as sodium citrate $0.6H_2O$. The calcium chloride-sodium citrate solution is thoroughly mixed until the ingredients are dissolved and this solution is added to the alginate mixture prepared above with vigorous stirring and immediately following, the total composition is poured into a dish or plate, frozen and lyophilized as set forth in Example 1 above.

The above descriptions and examples illustrate particular constructions including the preferred embodiments of the solutions. However, the invention is not limited to the precise constructions described herein, but, rather, all modifications and improvements thereof encompassed within the scope of the invention.

The alginate principally utilized in the examples described herein was one having an aqueous viscosity of 170 centepoise at 2.0% concentration. It is clear that other alginates having other viscosities may be utilized without deviating from the novelty of the revelations contained in this patent as long as the alginate is of a concentration and viscosity that can be reasonably poured into a mold when a calcium or other anion alginate precipitating molecule is added to the sodium alginate. The alginate that we have principally used in the example described herein was sodium alginate, but it is clear that other water soluble alginates may be utilized without deviating from the novelty of the invention described herein such as water soluble ammonium alginate, magnesium alginate, or potassium alginate.

It is well known in the profession that various glycols as plasticizers may be used to improve the flexibility of alginate films or fibers. The plasticizer that we have principally used in the examples described herein has been glycerine because of its low cost and because of its ready availability. It is clear however that other plasticizers may be utilized such as propylene glycol, or ethylene glycol without deviating from the novelty of the invention described herein.

In the example cited, we utilized sodium citrate as a sequestering agent for the calcium ion in order that the aqueous insoluble calcium alginate moiety not precipitate during the preliminary mixing, but that precipitation of calcium alginate is postponed for a suitable period of time to permit the mixture to be poured into a suitable mold or tray. However, sequestering agents other than sodium citrate may be utilized without deviating from the novelty of the invention described herein such as ethylenediamine tetra-acetic acid (EDTA).

In the examples cited herein, calcium chloride has been utilized to provide the calcium ion which precipitates the insoluble calcium alginate which also may serve to entrap into the calcium alginate matrix other components as described herein. It is clear, as has been mentioned, that other salts may be utilized to precipitate the alginate such as those of aluminum, zinc, copper, chromium, or silver and these insoluble alginates may readily be utilized to precipitate the coercive alginate-polymer mixtures described in the Examples provided herein without deviating from the essential merits of this invention. However, since the alginate compositions are to be utilized in and on biological tissues, the particular salt utilized to precipitate the alginate should be dictated by any restraints of toxicity or other untoward reactions that might result from their use for the preparation of bandages, dressings, or surgical products as herein described.

Note that in example 2, we utilized collagen as a component in the alginate mixture so that the insoluble calcium alginate gel will contain an agent which has hemostatic activity and therefore would serve to stem the flow of blood from a wound when a dressing containing collagen is placed thereon. However, it is clear that other medicinal agents may be incorporated into the sodium alginate mixture prior to its being precipitated as a sodium alginate gel which medicinal agents serve to treat a wound by slowing being released from the insoluble calcium alginate moiety either by osmosis or by the gradual slow dissolution of the calcium alginate gel, and such medicinal agents can be incorporated into the mixture without deviating from the novelty of the invention

described herein, such as anti-inflammatory agents, antibiotics, and anti-bacterial agents.

Many of the examples described herein utilize the surface active agents such as those characterized as Tween 80, aerosol OT-B, or Pluronic L64. These surface-active agents are utilized primarily to effect a dispersion between the non-aqueous miscible components utilized in achieving a coercive mixture with the aqueous soluble sodium alginate in order to insure a homogenuity throughout the solutions that are then precipitated as insoluble alginate compositions.

These surface active agents are also utilized in order to improve the wetting of a medical dressing or bandage in the event that a wound may be exudating, and the enhanced wicking in such a bandage or medical dressing serves to quickly absorb any blood or serum from a wound.

It is clear that other surface active agents may be used for these purposes without deviating from the novelty of the invention described herein.

In order to enhance the retention of our alginate gelled composition in or on tissues, we have prepared either as coacervates or covalently linked substances which would tend to enhance the insoluble property of the calcium alginate moiety for extended periods of time by utilizing agents such as stytens butadiene copolymer latex or a melamine-formaldehyde condensate or a wax micro particle dispersion as set forth in the examples. However, it is clear that other insoluble moieties may be utilised as coacervates or covalently linked to the alginate molecule which would serve to enhance the longevity in tissues of the dressing or implants so utilized without deviating from the novelty from the invention described herein.

I claim:

1. A method of making a water-insoluble alginate sponge or foam product to be utilized in the preparation of wound dressings or surgical products comprising the steps of:

(I) mixing together, to form a composite liquid mixture, a first liquid mixture comprising:

(a) an aqueous solution of a water soluble alginate composition with a water soluble sequestering agent;

(II) adding to the mixture (I) a plasticizer and a surface active agent;

(III) while allowing the total composition of (I) and (II) to be mixed vigorously, adding a di- or trivalent metal ion capable of complexing the water-soluble alginate to form water-insoluble alginate hydrogels;

(IV) pouring said composite liquid mixture into a dish or tray until the water-insoluble alginate hydrogel forms;

(V) placing said insoluble alginate hydrogel form contained in a tray or dish into a freezer until the composite insoluble alginate hydrogel is frozen;

(VI) lyophilizing said frozen composite insoluble alginate hydrogel until all of the moisture has been removed.

2. A method of making a water-insoluble alginate sponge or foam product to be utilized in the preparation of wound dressings or surgical products comprising the steps of:

(I) mixing together, to form a composite liquid mixture, a first liquid mixture comprising:

(a) an aqueous solution of a water soluble alginate composition with a water soluble sequestering agent;

(II) adding to the mixture (I) a plasticizer, a surface active agent, and a suitable medicinal agent for the treatment of wounds;

(III) while allowing the total composition of (I) and (II) to be mixed vigorously, adding a di- or trivalent metal ion capable of complexing the water-soluble alginate to form water-insoluble alginate hydrogels;

(IV) pouring said composite liquid mixture into a dish or tray until the water-insoluble alginate hydrogel forms;

(V) placing said insoluble alginate hydrogel form contained in a tray or dish into a freezer until the composite insoluble alginate hydrogel is frozen;

(VI) lyophilizing said frozen composite insoluble alginate hydrogel until all of the moisture has been removed.

3. A method of making a water-insoluble alginate sponge or foam product to be utilized in the preparation of wound dressings or surgical products comprising the steps of:

(I) mixing together, to form a composite liquid mixture, a first liquid mixture comprising:

(a) an aqueous solution of a water soluble alginate composition with a water soluble sequestering agent;

(II) adding to the mixture (I) a plasticizer, a surface active agent, and an aqueous insoluble agent that can form a coacervate with a water-insoluble alginate hydrogel;

(III) while allowing the total composition of (I) and (II) to be mixed vigorously, adding a di- or trivalent metal ion capable of complexing the water-soluble alginate to form water-insoluble alginate hydrogels;

(IV) pouring said composite liquid mixture into a dish or tray until the water-insoluble alginate hydrogel forms;

(V) placing said insoluble alginate hydrogel form contained in a tray or dish into a freezer until the composite insoluble alginate hydrogel is frozen;

(VI) lyophilizing said frozen composite insoluble alginate hydrogel until all of the moisture has been removed.

4. A method of making a water-insoluble alginate sponge or foam product to be utilized in the preparation of wound dressings or surgical products comprising the steps of:

(I) mixing together, to form a composite liquid mixture, a first liquid mixture comprising:

(a) an aqueous solution of a water soluble alginate composition with a water soluble sequestering agent;

(II) adding to the mixture (I) a plasticizer, a surface active agent, and a water soluble agent than can chemically cross-link with the alginate moiety to form an aqueous-insoluble complex;

(III) while allowing the total composition of (I) and (II) to be mixed vigorously, adding a di- or trivalent metal ion capable of complexing the water-soluble alginate to form water-insoluble alginate hydrogels;

(IV) pouring said composite liquid mixture into a dish or tray until the water-insoluble alginate hydrogel forms;

(V) placing said insoluble alginate hydrogel form contained in a tray or dish into a freezer until the composite insoluble alginate hydrogel is frozen;

(VI) lyophilizing said frozen composite insoluble alginate hydrogel until all of the moisture has been removed.

5. The method of making a water-insoluble alginate sponge or foam product as recited in claim 1 wherein said water-soluble alginate is selected from a group consisting of ammonium, magnesium, potassium, and sodium salts of alginate.

6. The method of making a water-insoluble alginate sponge or foam product as recited in claim 1, wherein said di- or trivalent metal salt is selected from a group consisting of calcium, zinc, aluminum, copper, chromium, or silver.

7. The method of making a water-insoluble alginate sponge or foam product as recited in claim 1, wherein said surface active agent is selected from a group consisting of Tween 80, Aerosol O-TV or pluronic L64.

8. The method of making a water-insoluble alginate sponge or foam product as recited in claim 1, wherein said

plasticizer is selected from a group consisting of sodium citrate, ethylenediamine tetra-acetic acid.

9. The method of making a water-insoluble alginate sponge or foam product as recited in claim 2, wherein said suitable medicinal agent is selected from a group consisting of antibiotics, collagen, antimicrobial agents, and anti-inflammatory agents.

10. The method of making a water-insoluble alginate sponge or foam product as recited in claim 3, wherein said aqueous insoluble agent that can form a coacervate with a water-insoluble alginate hydrogel is selected from a group consisting of waxes, lipids, and latex particles.

11. The method of making a water-insoluble aginate sponge or foam product as recited in claim 4, whereas said water soluble agent that can chemically cross-link with the alginate moiety is selected from a group consisting of melamine formaldehyde cross-linking agent.

12. A water-insoluble alginate sponge or foam wound dressing prepared by the method of claim 1.

13. A water-insoluble alginate sponge or foam wound dressing prepared by the method of claim 2.

14. A water-insoluble alginate sponge or foam wound dressing prepared by the method of claim 3.

15. A water-insoluble alginate sponge or foam wound dressing prepared by the method of claim 4.

16. A water-insoluble alginate sponge or foam wound dressing prepared by the method of claim 5.

17. A water-insoluble alginate sponge or foam wound dressing prepared by the method of claim 6.

18. A water-insoluble alginate sponge or foam wound dressing prepared by the method of claim 7.

19. A water-insoluble alginate sponge or foam wound dressing prepared by the method of claim 8.

20. A water-insoluble alginate sponge or foam wound dressing prepared by the method of claim 9.

21. A water-insoluble alginate sponge or foam wound dressing prepared by the method of claim 10.

22. A water-insoluble alginate sponge or foam wound dressing prepared by the method of claim 11.

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